BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents *will not* correct images, please do not report the images to the Problem Image Mailbox.

Med. Sci. Res., 1988; 16, 685-686

Anti-cataract effect of t pical quercetin and myricetin in galact semic rats

Madan Mohan, S.K. Gupta, S. Agnihotri, S. Joshi and A.K. Uppal

Division of Ocular Pharmacology, Dr Rajendra Prasad Centre for Ophthalmic Sciences, All-India Institute of Medical Sciences, New Delhi-110 029, India

The role of aldose reductase (AR) in the causation of diabetic cataract is now well established [1]. One major finding to support the role of AR in sugar cataract is the prevention and delay in the progression of cataract development by certain AR inhibitors [2–4]. Flavonoids have been reported to be potent inhibitors of lens AR [5, 6]. Of these, quercetin and myricetin have been shown to be more potent in comparison with others [7]. So far only limited attempts have been made to evaluate the efficacy of these flavonoids as anti-cataract agents [8]. In the present study the effect of topical quercetin and myricetin in galactosemic cataracts was assessed.

Materials and methods: Galactose cataracts were induced in young albino rats (60–80 g b.wt) maintained in standard laboratory conditions. Animals were fed a diet containing 30% galactose and were randomly divided into three groups of 12 rats each. Group 1 served as control. In group 2 and 3 animals, quercetin (0.5%) and myricetin (0.1%) eye drops were applied, respectively. The eye drops were prepared fresh every 3rd day in 0.5% methylcellulose and were applied three times a day in both the eyes of the experimental animals while the vehicle was applied in the control group.

The stages of cataract (1 to 5) were graded according to the classification of Sippel [9] as described below:Stage 1A, thin band of vacuoles in the periphery;Stage 1B, vacuoles increase and occupy one third of the lens in anterior cortex;Stage 1C, vacuoles occupy two thirds of the lens;Stage 2, vacuoles now reach the centre of the lens and liquefication of vacuoles begins; Stage 3, vacuoles have liquefied and a uniform opalescence develops; Stage 4, nuclear opacification begins; Stage 5, total involvement of lens.

The eyes were examined every alternate day by the slit lamp retro-illumination technique. Morphological changes in drug treated groups were compared with the control group. Percent reduction in the numbers of animals developing cataracts or the delay in reaching the different stages of cataractogenesis was considered as the anti-cataract effect.

Six rats from each group were killed by decapitation on the 10th day of galactose feeding and their lenses removed for dulcitol assay. In the remaining animals the diet and drug treatment schedule were continued for a further 30 days when all the animals were killed and their lenses dissected out for an assessment of their dulcitol content by the method of West and Rapoport [10]. Blood glucose and galactose levels were measured by the method of Huffman [11].

Results and discussion: The anti-cataract action of quercetin and myricetin was assessed by comparing the percentage of eyes developing cataract and the stage-wise progression of cataract formation in drug and vehicle treated eyes when subjected to cataractogenic challenge. The results are shown in Table 1. The onset and cataract development were significantly delayed in the eyes treated topically with quercetin or myricetin. On the 4th day, 50% of the quercetin treated eyes and 75% of the myricetin treated eyes were normal whereas 100% of the eyes in the control group had developed a thin band of peripheral opacities (stage 1A). Besides delay in the onset, development of cataract appeared to be slower in the treated eyes. By the 30th day, 100% of eyes in the control group had developed nuclear opacity (stage 4) while the eyes in the treated groups had progressed to stage 2 only. The stages of eyes in all the three groups remained stationary till the 40th day. Statistical analysis by χ^2 test indicated that the differences were highly significant ($p < 0.001$).

Table 1: Anti-cataract effect of topical quercetin and myricetin on the development of cataracts in rats (number of eyes in each group = 24)

Groups	Stage of cataract	Number of eyes on different days of galactose feeding					
		4	8	14	19	30	40
Control	N*	–	–	–	–	–	–
	1A	24	–	–	–	–	–
	1B	–	24	2	–	–	–
	1C	–	–	22	–	–	–
	2	–	–	–	24	–	–
	3	–	–	–	–	–	–
	4	–	–	–	–	24	24
	5	–	–	–	–	–	–
Quercetin (0.5%)	N	12**	–	–	–	–	–
	1A	12**	24**	8*	–	–	–
	1B	–	–	16**	16**	–	–
	1C	–	–	–	–	–	–
	2	–	–	–	8**	24**	24**
	3	–	–	–	–	–	–
	4	–	–	–	–	–	–
	5	–	–	–	–	–	–
Myricetin (0.1%)	N	18**	–	–	–	–	–
	1A	6**	24**	6*	–	–	–
	1B	–	–	18**	–	–	–
	1C	–	–	–	24**	–	–
	2	–	–	–	–	24**	24**
	3	–	–	–	–	–	–
	4	–	–	–	–	–	–
	5	–	–	–	–	–	–

*N = normal lens. In comparison with control, p <: *0.01; **0.001.

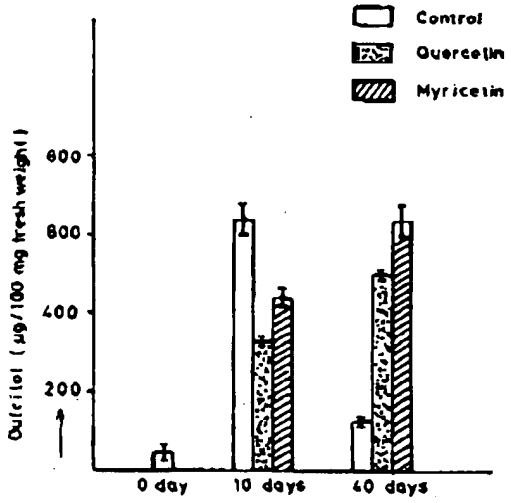

Figure 1: Changes in dulcitol content in controls and in quercetin or myricetin treated lenses at different days of galactose feeding (means ± SEM).

Biochemical studies showed that on the 10th day the level of dulcitol, the polyalcohol product of galactose, was significantly higher in the lenses of the control group as compared with the quercetin and myricetin treated groups ($p < 0.001$, $p < 0.05$, respectively). However, on the 40th day when the control lenses were in stage 4 of cataract, the dulcitol content was found to be less than that in the treated lenses (Figure 1) owing to excessive hydropic swelling and rupturing of lens fibres in the untreated eyes. On the same day, early stages of cataract and higher levels of dulcitol in the treated groups suggested a slower progression of cataract.

Blood glucose and galactose levels were found to be elevated in all the three groups; however, the difference was not significant. No ocular toxicity was observed during the study period. It is concluded that quercetin and myricetin may prove to be potential anti-cataract agents.

1. Kinoshita, J.H. (1986) *Am. J. Ophthalmol.*, 102, 685-692
2. Duquesne, N.S., Gresalfa, E., Gonzalez, R. and Dvornik, D. (1985) *Proc. Soc. Exp. Biol. Med.*, 178, 599-605
3. Kador, P.F., Akagi, Y. and Kinoshita, J.H. (1986) *Metabolism*, 35, 15-19
4. Stribling, D., Marriage, D.J., Harrison, H.E. and Earl, D.C.N. (1985) *Metabolism*, 34, 336-344
5. Varma, S.D., Mikuni, I. and Kinoshita, J.H. (1975) *Science*, 188, 215-216
6. Varma, S.D., Mizuno, A. and Kinoshita, J.H. (1977) *Science*, 195, 205-206
7. Varma, S.D. and Kinoshita, J.H. (1976) *Biochem. Pharmacol.*, 25, 2505-2511
8. Bayer-Mears, A. and Farnsworth, P.N. (1979) *Exp. Eye Res.*, 28, 709-716
9. Sippel, T.O. (1966) *Invest. Ophthalmol.*, 5, 568-575
10. West, C.D. and Rapoport, S. (1949) *Proc. Soc. Exp. Biol.*, 70, 142
11. Hultman, E. (1974) in *Clinical Biochemistry Principles and Methods* (Curtius, H.Ch. and Roth, M., eds), vol. II, pp. 908-930, Walter de Gruyter, E., Berlin, New York

This study was supported by the Indian Council of Medical Research.

Reprint requests to: Dr S.K. Gupta, Division of Pharmacology, Dr R.P. Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi-110029, India.

Paper received: 12th April, 1988; amended 1st June, 1988